

DECLARATION

I, William Roger Buckett, a British Subject of 27 Trevor Road, West Bridgford, Nottingham, England, do hereby declare that:-

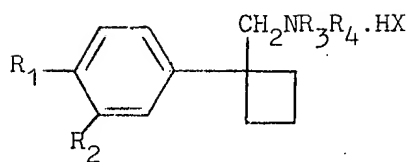
1) In 1959 I was awarded the degree of B. Pharm. with Honours in Pharmacology by the University of London, England. In 1965 I was awarded the degree of Ph.D. in Pharmacology from the University of London. In 1983 the same university awarded me a higher doctorate, namely the D.Sc. degree, on the basis of my published work in diverse areas of neuropharmacology. In addition I have been designated Fellow of the Institute of Biology (F.I. Biol.) and of the Pharmaceutical Society of Great Britain (F.P.S.). From 1960 to date I have been employed in industrial pharmacology in several companies including Organon Laboratories Ltd., and ICI PLC, Pharmaceuticals Division (England), Novo Industri A/S (Denmark) and Centre de Recherche Merrell International (France). In 1980 I joined the Research Department of The Boots Company PLC, Nottingham, England as Section Leader (Mental Illness, Biology). In 1982 I was appointed Research Project Leader (Mental Illness) and in 1984 became Senior Section Leader (Mental Illness Projects). I am in charge of a team of scientists engaged in neuroscience research and am project leader for antidepressant, neuroleptic and antiepileptic projects. I have published over 75 papers and abstracts in scientific journals and am entirely familiar with the pharmacological and biochemical methods used to evaluate antidepressant drug activity in chemical compounds.



2) I am familiar with the compounds described in the present patent application which is a continuation of US Patent Application Serial No. 365285 and with the results which have been obtained for those compounds in the reserpine reversal test described on page 19 of the present application. The compounds exemplified in the present application give an ED50 figure of 30 mg/kg or less in the above test. When tested at a dose of 30 mg/kg the percentage reversal of these compounds exceeds 50%.

3) I am aware of and have read British Patent Specification 973,887 to Farbwerke Hoechst Aktiengesellschaft which discloses compounds having central-analeptic properties.

4) In experiments performed at my request and by staff under my supervision several compounds falling within the scope of the claims of British Patent Specification 973,887 have been tested in the reserpine reversal test described on page 19 of the present application and the results are given in Table I below.

Table I



	R_1	R_2	NR_3R_4	X	dose (mg/kg)	% reversal	Mean
A	H	OMe	NH_2	Cl	30 60	25,8,5 1,0	13 1
B	H	OMe		Cl	10 30 60	2 46,41,37,24 27,15	2 37 21
C	H	OH		Cl	30 60	22,15,17 *	18
D	H	H	NH_2	Cl	30 60	9,11,-7 12,22	4 17
E	OMe	OMe	NH_2	Cl	30 60	3,3,6 6,12	4 9
F	OMe	OMe	NPr_2	Cl	30 60	2,11 28,11	7 20
G	OH	OH	NH_2	Br	30 60	4,4 -3,2	4 -1
H	OH	OH	NPr_2	Br	30 60	6,-1 0,3	3 2


* Toxic effects seen with two out of ten animals dying.

5) The results given in Table I show that at a dose of 30 mg/kg none of the compounds gave a percentage reversal of 50% or greater. This is indicative of an ED50 of more than 30 mg/kg. It did not prove possible to calculate an ED50 figure because the response did not appear in many cases to be dose related. It would be expected that the percentage reversal would be greater when a dose of 60 mg/kg was administered than when a dose of 30 mg/kg was administered. The fact that this was not observed is due to the toxicity of these compounds at the higher dose as is shown by the results for compound C in which two of the ten test animals died during the experiment.

6) I have reviewed the results given in Table I and I would not expect any of the compounds A to H listed therein to show antidepressant activity.

Further declarant sayeth not

I, the undersigned declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States code and that such wilful false statements may jeopardise the validity of the application or any patent issuing thereon.


William Roger Buckett

Signed at Nottingham, England on the 15th day of
October, 1984.